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Bjorn Frendeus

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EXAMINER

STEELE, AMBER D

ART UNIT

PAPER NUMBER

1639

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DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/526,695	Applicant(s) FRENDUEUS, BJORN	
	Examiner Amber D. Steele	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on August 26, 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31-59 is/are pending in the application.
- 4a) Of the above claim(s) 32, 33 and 55-59 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 31 and 34-54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 March 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/8/06; 3/3/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

1. The preliminary amendment received on March 3, 2005 canceled claims 1-30 and added new claims 31-59.

Claims 31-59 are currently pending.

Claims 31 and 34-54 are currently pending.

Election/Restrictions

2. Applicant's election with traverse of Group I (wet bench method; claims 31, 34-38, and 40-54) in the reply filed on August 26, 2008 is acknowledged. The traversal is on the ground(s) that Groups I and II should be rejoined as they are linked as to form a single general inventive concept because the equation of claim 39 is derived from the equation of claim 38. This is found persuasive for Groups I and II only. Applicants also asserted that Groups III and IV should also be rejoined (i.e. Groups III and IV should be one Group). However, it is noted that Groups III and IV are nonelected inventions and Groups III and IV require automation regarding the equations (i.e. computer process).

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 32-33 and 55-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **with** traverse in the reply filed on August 26, 2008.
4. Upon further consideration, the species requirement is withdrawn.

Priority

5. The present application claims status as a National Stage application (i.e. 371) of PCT/EP03/09991 filed September 3, 2003. The present application also claims foreign priority to UK 0220506.0 filed September 4, 2002.

Information Disclosure Statement

6. The information disclosure statement filed March 3, 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

7. The information disclosure statement (IDS) submitted on March 8, 2006 is being considered by the examiner.

Specification

8. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Invention as Claimed

9. A method of isolating at least one anti-ligand to at least one target ligand comprising the steps of: (i) providing a library of anti-ligands, (ii) providing an amount of a first subtractor ligand, (iii) providing an amount of a second target ligand, (iv) determining amounts of first subtractor and second target ligands using one or more equations derived from the universal law

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of mass action (see present claim 31 for equation), (v) providing the amount of the first subtractor ligand determined in step (iv), (vi) providing the amount of the second target ligand determined in step (iv), (vii) providing separation means for isolating anti-ligand bound to the second target ligand from anti-ligand bound to the first subtractor ligand, (viii) exposing the library of (i) to the ligands of (v) and (vi) to permit binding of anti-ligands to ligands, and (ix) isolating the anti-ligand bound to the second target ligand with the separation means and variations thereof.

10. The functional limitation of “subtractor” regarding the ligand is not provided patentable weight. See MPEP § 2114h . Applicants may wish to include a negative selection method step into the present claims. However, applicants are cautioned against adding new matter to the claims.

Claim Objections

11. Claims 34-36, 38-40, 43, 47, 50, and 52-54 objected to because of the following informalities: the claims are dependent on claims drawn to a nonelected invention (i.e. claims 32 and/or 33). Appropriate correction is required.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 31 and 34-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the

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scope of the presently claimed invention. Independent claim 31 reads “a first subtractor ligand” and “a second target ligand”. However, the claims do not discuss a second subtractor ligand or a first target ligand. Therefore, it is not clear if more than one subtractor ligands or more than one target ligands are required by the presently claimed method.

13. Claims 31 and 34-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. One of skill in the art would not be able to determine the scope of the presently claimed invention. Independent claim 31 discusses a separation means in steps (vii) and (ix), due to antecedent basis in method step (ix), it appears that the separation means must be the same in both method steps. However, dependent claims 40-49 suggest that different separation means may be utilized.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

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reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

15. Claims 31, 34-35, and 38-54 are rejected under 35 U.S.C. 102(e) as being anticipated by Lonberg et al. U.S. Patent 7,135,287 (371 date of April 1, 2002; effective filing date of October 2, 1999).

For present claims 31, 34-35, and 38-39, Lonberg et al. teach display selection methods to screen libraries of human immunoglobulins comprising: (i) providing a library of antibodies, ii-iii) providing ligands including ligands for negative selection, prescreening, and/or targets including antigens, (iv-vi) utilizing the universal law of mass action to determine the amount of ligands, (vii) separating antibodies from ligands, and (viii-ix) repeating the selection and separation steps (please refer to the entire specification particularly the abstract; columns 1-4, 7, 10, 15-28, and 30; Examples 13, 20-21, 26, and 35). Regarding the equations in claims 31 and 38-39, since applicants elected a wet bench method, these steps equate to a mental process (i.e. mathematical manipulation). See MPEP § 2111 and *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969).

For present claims 40-42 and 45-46, Lonberg et al. teach cell membranes and cell vesicle screening (please refer to the entire specification particularly Example 26).

For present claims 43-44 and 47-49, Lonberg et al. teach different densities, density centrifugation, and sucrose gradients (please refer to the entire specification particularly columns 24, 26-27, 30; Examples 13).

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For present claims 50-51, Lonberg et al. teach phage display (please refer to the entire specification particularly columns 18-21; Examples 5-8, 11, 13).

For present claims 52-53, Lonberg et al. teach antigens and antibodies (please refer to the entire specification particularly columns 4, 20-28; Examples 13, 15-21, 23-25, 34-35).

For present claim 54, Lonberg et al. teach stimulating cells to produce antigens or antibodies (please refer to the entire specification particularly columns 15-16; Examples 13, 15-16, 23-25, 34-35).

Therefore, the teachings of Lonberg et al. anticipate the presently claimed method.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

17. Claims 31 and 34-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lonberg et al. U.S. Patent 7,135,287 (371 date of April 1, 2002; effective filing date of October 2, 1999) and Marks et al. U.S. Patent 6,794,128 (filed February 12, 1999; effective filing date of April 24, 1998).

For present claims 31, 34-35, and 38-39, Lonberg et al. teach display selection methods to screen libraries of human immunoglobulins comprising: (i) providing a library of antibodies, ii-iii) providing ligands including ligands for negative selection, prescreening, and/or targets including antigens, (iv-vi) utilizing the universal law of mass action to determine the amount of ligands, (vii) separating antibodies from ligands, and (viii-ix) repeating the selection and separation steps

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(please refer to the entire specification particularly the abstract; columns 1-4, 7, 10, 15-28, and 30; Examples 13, 20-21, 26, and 35). Regarding the equations in claims 31 and 38-39, since applicants elected a wet bench method, these steps equate to a mental process (i.e. mathematical manipulation). See MPEP § 2111 and *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-51 (CCPA 1969).

For present claims 40-42 and 45-46, Lonberg et al. teach cell membranes and cell vesicle screening (please refer to the entire specification particularly Example 26).

For present claims 43-44 and 47-49, Lonberg et al. teach different densities, density centrifugation, and sucrose gradients (please refer to the entire specification particularly columns 24, 26-27, 30; Examples 13).

For present claims 50-51, Lonberg et al. teach phage display (please refer to the entire specification particularly columns 18-21; Examples 5-8, 11, 13).

For present claims 52-53, Lonberg et al. teach antigens and antibodies (please refer to the entire specification particularly columns 4, 20-28; Examples 13, 15-21, 23-25, 34-35).

For present claim 54, Lonberg et al. teach stimulating cells to produce antigens or antibodies (please refer to the entire specification particularly columns 15-16; Examples 13, 15-16, 23-25, 34-35).

However, Lonberg et al. does not specifically teach utilizing an excess of one ligand over another ligand.

For present claims 36-37, Marks et al. teach methods of selecting phage displayed antibodies comprising contacting target cells with a phage display antibody library and also contacting the phage display antibody library with subtractive cells wherein the subtractive cells

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are in at least a 2 fold excess of the target cells and including 100 fold or 1000 fold excess (please refer to the entire specification particularly the abstract; columns 2-3, 12-13, 15, 18-19, 39; claims 1-42).

The claims would have been obvious because a particular known technique (i.e. subtractive screening of an antibody phage displayed library with 100 fold excess of subtractor to target as taught by Marks et al.) was recognized as part of the ordinary capabilities of one skilled in the art. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Conclusion

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Mandecki et al., 1995, A Mathematical Model for Biopanning (Affinity Selection) Using Peptide Libraries on Filamentous Phage, J. Theor. Biol., 176: 523-530 (please note: the present reference was cited on the IDS received on March 3, 2005, however a copy was not provided).

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Patent Examiner, Art Unit 1639

November 14, 2008